REMARKS

Reconsideration of the application in view of the above amendments and the following remarks is respectfully requested.

Claims 1, 7-9 and 11-12 were pending in the subject application. Claim 9 is rewritten in independent form by incorporating the language of claim 1. Support for the amendment is found, for example, in claims 1 and 9, and at page 9, lines 27-29, of the subject application. Claims 1, 7 and 8 are now cancelled without prejudice to prosecute in a related application. With the cancellation of claims 1, 7 and 8, the dependencies of claims 11 and 12 are amended to delete reference to claims 1, 7 and 8. No new matter has been added by the amendments to the claims. Therefore, amended claims 9 and 11-12 are now pending in the subject application, with claim 9 as the only independent claim.

In the Office Action dated March 26, 2003, claims 1, 7, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Disis et al. (J. Immunol. 156:3151-3158, May 1996) in view of Mamula et al. (J. Immunol. 152:1453-1461, 1994) and any one of Dyrberg et al. (Current Topic in Microbiology and Immunology 130:25-37, 1986), or Mamula et al. (J. Immunol. 149:789-795, 1992), or Fedoseyeva et al. (Transplantation 61:679-683, 1996), or Mahi-Brown et al. (J. Reproductive Immunology 21:29-46, 1992).

Applicants neither agree with nor acquiesce to, this rejection of claims 1, 7, 11 and 12. However, since claims 1 and 7 have been cancelled without prejudice in order to expedite allowance of claim 9 (and claims 11-12 have been amended to no longer depend from claims 1 and 7), this rejection has been rendered moot. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7-9, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over the references applied to claims 1, 7, 11 and 12 above, and further in view of Spitler et al. (U.S. Patent No. 5,925,362).

Applicants neither agree with nor acquiesce to, this rejection of claims 1, 7 and 8. However, since claims 1, 7 and 8 have been cancelled without prejudice in order to expedite allowance of claim 9 (and claims 11-12 have been amended to no longer depend from claims 1, 7 and 8), this rejection has been rendered moot, except for claim 9 and claims 11-12 which depend therefrom. Withdrawal of this rejection as applied to claims 1, 7 and 8 is respectfully requested.

With respect to claim 9 (which has been rewritten in independent form) and claims 11-12 which depend therefrom, Applicants respectfully, but strenuously, traverse this rejection. Claims 9 and 11-12 were rejected under Section 103(a) as unpatentable over Disis et al. in view of Mamula et al. (1994) and any of Dyrberg and Oldstone, or Mamula et al. (1992), or Fedoseyeva et al., or Mahi-Brown et al., and further in view of Spitler et al. Applicants agree that Disis et al. teaches that immunologic tolerance to self tumor antigens represents a potential barrier to effectively vaccinating against tumor antigens, and that Disis et al. does not teach or suggest Applicants' claimed invention of eliciting or enhancing a T cell response to a human tumor self antigen. However, the deficiencies in the teachings of Disis et al. (relative to Applicants' claimed invention) were asserted in the Office Action to be supplied in part by Mamula et al. (1994). Applicants respectfully disagree.

At page 2 of the Office Action, Mamula et al. (1994) is asserted to "teach that foreign proteins which have cross-reacting determinants generate auto-antigen presenting B cells which can activate an autoimmune T-cell response"; and at page 5 of the Office Action, Applicants' attention is directed to Figure 5 of Mamula et al. as evidence to prove the Office Action's characterization of the reference. Applicants respectfully point out that this characterization in the Office Action of Mamula et al. is incomplete and therefore inadvertently misleading. What is missing from the characterization of Mamula et al. in the Office Action is the fact that Mamula et al. immunized with <u>self</u> antigen (self snRNPs) in order for the B cells to activate an autoimmune T cell response. More specifically, near the end of the abstract at page 1453 of Mamula et al. it is stated: "To address this hypothesis [that breaking T cell tolerance to self snRNPs was dependent on cross-reactive B cells], B cells purified from mice immunized with recombinant human A protein were transferred into naïve mice. Upon boosting with native mouse snRNPs, autoreactive $CD4^+$ T cells specific for mouse Ags, and not cross-reactive with

human snRNPs, were observed." Thus, in Mamula et al. there was a step of boosting with self snRNPs. Similarly, in part A of the legend for Figure 5, it is stated: "Cells were adoptively transferred into naïve recipient mice followed by immunized with mouse snRNPs (see *Materials and Methods*)." In the section of the Materials and Methods that begins at the bottom of page 1454 and concludes at the top of page 1455 of Mamula et al., it is stated that mice receiving B cells by adoptive transfer were "then immunized at the base of the tail and in the footpad with a total of 50 μg of murine snRNPs in CFA (method used in Figure 5, A and B)." Thus, immunization with self antigen (self snRNPs) was included in Mamula et al. in order for B cells to activate an autoimmune T cell response. This is not Applicants' claimed invention which does not require immunizing with self antigen. Mamula et al. (at page 1455, left column, last paragraph) teaches that immunization with foreign snRNPs alone elicits T cell responses to foreign snRNPs but not to self snRNPs. Therefore, absent the inclusion of immunization with self antigen (which is not required in Applicants' invention as claimed), Mamula et al. does not teach that foreign proteins can generate B cells that can activate an autoimmune T cell response. Accordingly, Mamula et al. (1994) does not support a case for *prima facie* obviousness of Applicants' claimed invention under Section 103(a).

Further, the remaining cited references, taken with Disis et al. individually or in any combination, do not establish a *prima facie* case for obviousness under Section 103(a). At the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully elicit or enhance a T cell response to prostatic acid phosphatase (PAP) using Applicants' method as claimed. Dyrberg et al. focuses on the initiation of autoimmune responses by foreign pathogens, particularly induction by viruses. Mamula et al. (1992) discloses the use of cytochrome c to initiate autoimmune responses. Fedoseyeva et al. focuses on elucidating the immune mechanisms underlying long term allograft rejection following transplantation. Mahi-Brown et al. discloses the cellular immune response to immunization with zona pellucida antigens. None of these references provides any teaching regarding tumor self antigens in general nor PAP in particular. Tumor self antigens in general (and HER-2/neu and PAP as particular species) present unique difficulties in attempting to generate an autoimmune T cell response, as discussed by Disis et al. At the time of Applicants'

invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply these teachings, that do not concern a tumor self antigen, to PAP to successfully elicit or enhance a T cell response to PAP.

Claim 9 (and therefore claims 11-12 which depend therefrom) recites in part "with an amino acid sequence native to a non-human source". Spitler et al. does not teach or suggest immunizing with an amino acid sequence native to a non-human source. Although Spitler et al. discloses PAP as a vaccine target, none of the cited references (individually or collectively) when combined with Spitler et al. provided, at the time of Applicants' invention, a reasonable expectation of success for the invention as claimed in the subject application. More specifically, at the time of Applicants' invention, there was no reasonable expectation that one of ordinary skill in the art could successfully apply the non-tumor related teachings (of Dyrberg et al., Mamula et al., Fedoseyeva et al. or Mahi-Brown et al.) to PAP of Spitler et al.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness of claims 9 and 11-12 under Section 103(a).

Therefore, it is believed that this rejection of claims 9 and 11-12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7, 8, 11 and 12 were rejected under 35 U.S.C. § 102(e) as unpatentable over Carson et al. (U.S. Patent No. 5,679,647) as evidenced by Mamula et al. (J. Immunol. 152:1453-1461, 1994).

Applicants neither agree with nor acquiesce to, this rejection of claims 1, 7, 8, 11 and 12. However, since claims 1, 7 and 8 have been cancelled without prejudice in order to expedite allowance of claim 9 (and claims 11-12 have been amended to no longer depend from claims 1, 7 and 8), this rejection has been rendered moot. Withdrawal of this rejection is respectfully requested.

In the Office Action, claims 1, 7-9, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Carson et al. (U.S. Patent No. 5,679,647) as evidenced by Mamula et al. (J. Immunol. 152:1453-1461, 1994) in view of Laus et al. (U.S. Patent No. 6,080,409).

Applicants neither agree with nor acquiesce to, this rejection of claims 1, 7, 8, 11 and 12. However, since claims 1, 7 and 8 have been cancelled without prejudice in order to expedite allowance of claim 9 (and claims 11-12 have been amended to no longer depend from claims 1, 7 and 8), this rejection has been rendered moot, except for claim 9 and claims 11-12 which depend therefrom. Withdrawal of this rejection as applied to claims 1, 7 and 8 is respectfully requested.

With respect to claim 9 (which has been rewritten in independent form) and claims 11-12 which depend therefrom, Applicants respectfully, but strenuously, traverse this rejection. Claims 9 and 11-12 were rejected under Section 103(a) as unpatentable over Carson et al. as evidenced by Mamula et al. (1994) in view of Laus et al. Applicants agree that Carson et al. does not teach PAP as a tumor associated antigen, and that Laus et al. teaches PAP as a tumor associated antigen. However, claims 9 and 11-12 were asserted in the Office Action to be unpatentable over Carson et al. "as evidenced by Mamula et al." (in view of Laus et al.). Applicants respectfully disagree.

At page 6 of the Office Action, Mamula et al. (1994) is purported to provide evidence for the rejection based on the assertion that Mamula et al. discloses that foreign proteins alone can activate an autoimmune T cell response via B cells. However, as discussed in detail above, Mamula et al. does not disclose that foreign proteins can activate an autoimmune T cell response in the absence of immunization with the self antigen. Applicants' claimed invention does not require immunizing with self antigen. Mamula et al. does not evidence that an autoimmune T cell response will be elicited when immunization is conducted in accordance with Applicants' claimed method (i.e., in the absence of a simultaneous or sequential immunization with self antigen).

Further, Carson et al. provides no evidence that a foreign protein alone can activate an autoimmune T cell response to a tumor self antigen. In particular, a review of Carson et al., including the Drawings and Examples, shows that no evidence is disclosed using a tumor self antigen. Carson et al. provides no reasonable expectation that one of ordinary skill in the art, at the time of Applicants' invention, using a foreign protein alone, could successfully generate an autoimmune T cell response to a tumor self antigen. Mamula et al. (1994) teaches the opposite,

that immunization with the self antigen is necessary for an autoimmune T cell response and that foreign protein alone is not sufficient.

Further, the teachings of Laus et al. provided no motivation with a reasonable expectation of success to generate an autoimmune T cell response to PAP using Applicants' claimed method. Laus et al. describes a method for inducing a T cell response by activating antigen presenting cells (APCs) *in vitro*. Activated APCs are then administered to induce a T cell response *in vivo*. This is a completely differently method than that described by Carson et al. or recited in Applicants' claims. In Laus et al., the ability of APCs, activated *in vitro*, to generate a T cell response *in vivo* following their administration, provided at the time of Applicants' invention no motivation with a reasonable expectation of success to generate an autoimmune T cell response to PAP by immunizing with a foreign protein or peptide (or a polynucleotide encoding either) that is homologous to PAP. Laus et al. also discloses that the compositions used to activate APCs *in vitro* can also be administered directly to an individual as a vaccine. However, the compositions of Laus et al. consist of a complex of a polypeptide antigen which is covalently linked to an APC binding protein. (Such a complex is formed by chemical means or recombinantly as a fusion protein. Exemplified is a PAP-GM-CSF fusion protein.) This is also completely different from Carson et al. or Applicants' claimed method, neither of which require as does Laus et al. that an antigen be covalently linked to an APC binding protein. The ability in Laus et al. of PAP covalently linked to an APC binding protein to generate a T cell response, provided at the time of Applicants' invention no motivation with a reasonable expectation of success to generate an autoimmune T cell response to PAP by immunizing with a foreign protein or peptide (or a polynucleotide encoding either) that is homologous to PAP.

As discussed herein, the teachings of Mamula et al. do not support a *prima facie* case for obviousness of Applicants' claimed invention over Carson et al. in view of Laus et al. Further, the teachings of Laus et al., which involve completely different methodology than in Carson et al., would not have provided one of ordinary skill in the art at the time of Applicants' invention with the motivation to substitute PAP into the method of Carson et al. with a reasonable expectation for success.

Accordingly, Applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case for obviousness under Section 103(a) of claim 9 and claims 11-12 which depend therefrom.

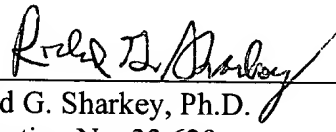
Therefore, it is believed that this rejection of claims 9 and 11-12 under 35 U.S.C. § 103(a) has been overcome. Withdrawal of this rejection is respectfully requested.

Therefore, in light of the amendments and remarks set forth above, Applicants believe all the Examiner's rejections have been overcome. Reconsideration of the application and allowance of all pending claims (9 and 11-12) are respectfully requested. If there is any further matter requiring attention prior to allowance of the subject application, the Examiner is respectfully requested to contact the undersigned attorney (at 206-622-4900) to resolve the matter.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



Richard G. Sharkey, Ph.D.
Registration No. 32,629

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